

Prediction of serious clinical outcomes in patients presenting with syncope in the short-term follow-up: Which variables to use?

Predicting clinical outcomes in syncope

İbrahim Ertaş¹, Derya Abuşka², Özgür Karcioğlu³¹ Department of Emergency Medicine, Faculty of Medicine, University of Yıldırım Beyazıt, Yenimahalle Research and Training Hospital, Ankara² Department of Emergency Medicine, Istanbul Research and Training Hospital, Istanbul³ Department of Emergency Medicine, Taksim Research and Training Hospital, Istanbul, Turkey

Abstract

Aim: This study aims to identify patient groups diagnosed with syncope in the emergency department (ED) based on initial evaluation, distinguish those whose etiology remains unclear necessitating hospitalization, and assess factors influencing serious clinical outcomes (SCOs) within 30 days post-ED admission for suspected syncope.

Material and Methods: This prospective, single-center observational study included patients presenting to the ED with suspected syncope over a six-month period. Subjects were categorized into three groups: those diagnosed and discharged following initial testing in the ED, those requiring hospitalization, and those undiagnosed in the ED but discharged for outpatient follow-up within 24 hours. The study's primary endpoint was the incidence of SCO, with secondary analysis focusing on determinants of SCO.

Results: The study encompassed 257 patients, among whom 22 (8.6%) experienced serious clinical outcomes (SCOs). The incidence of SCO was significantly higher at 22.2% among Group 2 patients, who required hospitalization, compared to those discharged directly from the emergency department (ED) ($p=0.013$). Notably, 62.9% of the hospitalized patients (Group 2) were diagnosed with cardiac syncope, while 11.1% had an undetermined cause of syncope despite ED evaluation. Abnormalities in electrocardiogram (ECG) were observed in 59.1% ($n=13$) of the patients who experienced SCOs ($p<0.001$).

Discussion: The data indicates a statistically significant increase in SCOs among patients admitted to the hospital compared to those discharged from the ED. Moreover, the presence of a normal ECG appears to correlate with a lower likelihood of experiencing SCOs, underscoring the value of ECG as a predictive tool in the assessment of syncope.

Keywords

Emergency Department, Electrocardiogram, Syncope, Serious Clinical Outcome

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Corresponding Author: İbrahim Ertaş, Department of Emergency Medicine, Faculty of Medicine, University of Yıldırım Beyazıt, Yenimahalle Research and Training Hospital, Ankara, Turkey. E-mail: ertasibrahim0880@gmail.com P: +90 506 440 08 80

Corresponding Author ORCID ID: <https://orcid.org/0000-0001-9375-4298>Other Authors ORCID ID: Derya Abuşka, <https://orcid.org/0000-0003-3527-2682> · Özgür Karcioğlu, <https://orcid.org/0000-0002-8814-6164>

This study was approved by the Ethics Committee of Istanbul Training and Research Hospital (Date: 2020-10-16, No: 2556)

Introduction

Syncope, defined as a transient loss of consciousness due to a brief reduction in cerebral perfusion, is marked by an abrupt onset and spontaneous resolution without the need for medical intervention [1-3]. This prevalent condition accounts for approximately 1-3% of emergency department (ED) visits annually, with one in four individuals experiencing at least one episode of syncope in their lifetime [4, 5].

The management of syncope is tailored to its underlying cause. In cases of cardiac syncope, the primary objective is to prevent sudden cardiac death. Conversely, when dealing with reflex syncope presented in the ED, the goals shift towards preventing future episodes, safeguarding against potential injury from falls during subsequent attacks, and enhancing the patient's quality of life [6].

Given the critical nature of timely and accurate patient assessments in emergency settings, the noisy and crowded environment of the ED can impair the evaluation process of patients at risk, underscoring the importance of utilizing algorithms in the assessment of such patients [7-9]. This approach not only streamlines patient care but also enhances the accuracy and efficiency of emergency medical interventions. In the ED, accurately assessing a syncope patient's risk for serious clinical outcomes (SCOs) is crucial. The European Society of Cardiology (ESC) 2018 Syncope Guidelines categorize patients based on their SCO risk into three levels: low-risk, high-risk, and intermediate-risk (neither high nor low) [10]. For low-risk patients, discharge from the ED is typically deemed safe. In contrast, high-risk patients are recommended for immediate emergency intervention and hospitalization. The intermediate-risk group warrants further investigations to address the potential for syncope recurrence.

This study aims to segregate patients admitted to the ED with a preliminary diagnosis of syncope into these risk categories based on initial evaluation, to analyze their 30-day SCO rates, and to identify factors influencing SCOs.

Material and Methods

This prospective observational study was conducted in the ED of a tertiary care hospital. Eligible participants were individuals aged 18 years and older who presented to the ED with a preliminary diagnosis of syncope between August 1, 2019, and February 1, 2020. Exclusion criteria included patients presenting with other causes of transient loss of consciousness such as seizures, vertigo, trauma, cerebrovascular events, drug intoxication, hypoglycemia, as well as pregnant women, individuals under 18 years of age, and those unwilling to provide consent for participation. Consent was obtained from all subjects participating in the study.

Upon presentation to the ED, all patients underwent a standardized initial evaluation, including a medical history review, physical examination, electrocardiography (ECG), and measurements of blood pressure in both supine and standing positions. Neuroimaging was conducted as needed for individuals suspected of experiencing a cerebrovascular event. Consistent with the ESC 2018 Syncope Guidelines, patients were stratified into three distinct groups for analysis [10]. The first group comprised patients who were evaluated, diagnosed,

and discharged directly from the ED. The second group included those who were either diagnosed with conditions requiring in-hospital treatment or undiagnosed but considered high risk for adverse outcomes, necessitating hospitalization. Criteria for high risk were established according to the ESC guidelines. The third group consisted of patients who remained undiagnosed after ED assessment but were clinically stable enough to be discharged within 24 hours for outpatient follow-up.

The primary outcome of interest was the occurrence of a SCO within 30 days of the ED visit. SCOs were defined as a recurrence of syncope, readmission to the ED, or mortality within this period. Follow-up for determining the 30-day SCOs was conducted via telephone calls to the patients or their relatives, using contact information collected at the time of ED admission. The analysis also explored factors potentially influencing the likelihood of an SCO, considered as a secondary endpoint.

Statistical analysis

Descriptive statistics of the dataset included mean, standard deviation, median, range (lowest to highest values), frequency, and proportion. The distribution normality of variables was assessed using the Kolmogorov-Smirnov test. For the analysis of independent quantitative data, the Kruskal-Wallis and Mann-Whitney U tests were employed. Independent qualitative data were evaluated using the Chi-square test, with Fisher's Exact test applied in instances where Chi-square test assumptions did not hold. All statistical analyses were conducted using SPSS software for Windows (Version 26, Chicago, IL, USA). Statistical significance was determined at a p-value of less than 0.05.

Ethical Approval

This study was approved by the Ethics Committee of Istanbul Training and Research Hospital (Date: 2020-10-16, No: 2556).

Results

After applying the exclusion criteria, 257 patients remained eligible for inclusion. Notably, the proportion of female patients was higher in Group 1 compared to the other two groups, and the mean age in this group was statistically significantly lower. The distribution of age and gender across the groups, along with vital signs analyses, is detailed in Table 1. Among the study participants, reflex syncope was identified in 51% (n=131) of patients, orthostatic syncope in 25.3% (n=65), and cardiac syncope in 10.9% (n=28). For 12.8% (n=33) of the patients, the type of syncope remained unspecified. Serious clinical outcomes were observed in 8.6% (n=22) of cases. The overall 30-day mortality rate across the cohort was 1.6% (n=4). Notably, the incidence of SCO was significantly higher in the group requiring hospitalization (p=0.013). The categorization of syncope types across the patient groups is detailed in Table 2. The mean age of patients experiencing SCO was 59.05±19.68 years, significantly older than those without SCO (p=0.017). Additionally, 68% (n=15) of patients with SCO were male; however, gender was not found to be a statistically significant factor in comparison to patients without SCO (p=0.078).

A prodromal period, characterized by symptoms such as dizziness, nausea, and sweating before syncope, was reported in 71.9% (n=185) of patients. SCOs occurred in only 3.2% (n=6) of patients with these prodromal symptoms, compared to

Table 1. Demographic data and vital signs of the groups

Demographic and vital data of patients		Group 1 (n=151)	Group 2 (n=27)	Group 3 (n=79)	P value
Age (years)	Mean ± SD	36.95 ±15.12	64.15±14.34	66.63±15.69	<0.001K
	Range	18-65	36-89	22-94	
Gender	Male	n=63 (41.7%)	n=17 (63%)	n=49 (62%)	0.005X ²
	Female	n=88 (58.3%)	n=10 (37%)	n=30 (38%)	
SBP (mmHg)	Mean ± SD	117.07±19.48	122.44±32.71	126.99±28.79	0.013A
	Range	70-183	65-204	77-220	
DBP (mmHg)	Mean ± SD	67.11±12.37	67.89±17.19	68.19±12.76	0.826A
	Range	41-132	42-127	42-113	
HR (/min)	Mean ± SD	82.16±11.96	84.11±22.69	79.01±23.69	0.307A
	Range	55-113	44-123	37-192	
BT (°C)	Mean ± SD	36.43±0.43	36.61±0.66	36.59±0.57	0.033A
	Range	36-39	36-40	35-39	
SatO2 (%)	Mean ± SD	97.42±1.43	96.11±1.82	96.66±1.73	<0.001A
	Range	92-99	92-99	90-99	
RR (/min)	Mean ± SD	14.62±1.15	15.85±1.72	15.43±1.54	<0.001A
	Range	Ara.18	13-20	13-22	
Glucose (mg/dL)	Mean ± SD	126.50±59.19	173.63±73.12	158.77±81.30	<0.001A
	Range	76-468	84-398	74-617	

SBP: systolic blood pressure, DBP: diastolic blood pressure, HR: heart rate, min: minute, BT: body temperature, SatO2: oxygen saturation, RR: respiratory rate, K: Kruskal-Wallis test, X²: Chi square test, A: One-Way ANOVA test.

Table 2. Distribution of syncope type and serious outcome among groups

		Group 1	Group 2	Group 3	P value
Syncope Type	Unknown	0	3 (11.1%)	30 (38%)	<0.001
	Reflex Syncope	123(81.5%)	0	8 (10.1%)	
	Orthostatic Syncope	28(18.5%)	7 (25.9%)	30 (38%)	
	Cardiac Syncope	0	17 (62.9%)	11 (13.9%)	
SCO		8 (5.3%)	6 (22.2%)	8 (10.1%)	0.013

Table 3. Electrocardiography (ECG) findings and distribution of serious outcomes among groups

		SCO		P value
		-	+	
Group 1	Normal ECG	135 (94.4%)	5 (62.5%)	0.013
	Abnormal ECG	8 (5.6%)	3 (37.5%)	
Group 2	Normal ECG	9 (42.9%)	1 (16.7%)	0.241
	Abnormal ECG	12 (57.1%)	5 (83.3%)	
Group 3	Normal ECG	36 (50.7%)	3 (37.5%)	0.479
	Abnormal ECG	35 (49.3%)	5 (62.5%)	
Normal ECG		180 (76.6%)	9 (40.9%)	<0.001
Abnormal ECG		55 (23.4%)	13 (59.1%)	

22.2% (n=16) of patients without them, indicating a significant association between the absence of a prodromal period and increased SCO risk (p<0.001). Electrocardiogram (ECG) results were normal in 73.5% (n=189) of study participants but showed abnormalities in 26.5% (n=68). The most frequent ECG abnormalities included atrial fibrillation (AF) at 7% (n=18), sinus bradycardia at 4.7% (n=12), and sinus tachycardia at 3.9% (n=10). ECG abnormalities were significantly more common in patients with SCOs (59.1%, n=13) than in those without (p<0.001). The distribution of ECG abnormalities and their correlation with SCOs are detailed in Table 3. Among patients experiencing SCOs, 59.1% (n=13) had ECG

abnormalities, with AF being the predominant finding (18.2%, n=4). Of the four deceased patients, ECGs revealed right bundle branch block (RBBB) in one case, AF in two, and sinus tachycardia in the remaining patient. Analysis of comorbid diseases among study participants revealed that hypertension (HT) at 28% (n=71), diabetes mellitus (DM) at 18.3% (n=47), and coronary artery disease (CAD) at 12.8% (n=33) were the most common. Among patients experiencing SCOs, the presence of HT, DM, CAD, and chronic obstructive pulmonary disease (COPD) did not significantly impact SCO incidence. However, patients with malignancy exhibited a notably higher SCO rate at 30% (n=4 out of 13), which was statistically significant (p=0.017). Echocardiography (ECHO) was performed for 20.6% (n=53) of patients, revealing mild heart failure in 3.9% (n=10), moderate heart failure in 0.4% (n=1), severe heart failure in 3.5% (n=9), very severe heart failure in 0.8% (n=2), and normal findings in 12.1% (n=31). The necessity for ECHO and the mean ejection fraction (EF) did not significantly predict SCOs, with no discernible difference in distribution across the groups (p=0.37). In the evaluation of laboratory results, blood lactate levels were assessed in 70 patients from Group 1, showing a significant relationship with SCOs. The average lactate level in patients without SCOs was 1.67±0.76 (n=65), compared to 2.06±1.59 in patients with SCOs (n=5), indicating higher lactate levels in those experiencing SCOs (p=0.032).

Discussion

Our study highlighted an increased incidence of serious clinical outcomes (SCOs) among hospitalized patients, predominantly those with cardiac syncope or undetermined syncope etiology in the emergency department (ED). This observation mirrors the findings of a large-scale multicenter study by Krishan RJ et al., which also reported a heightened SCO rate in hospitalized patients, attributed to both non-fatal arrhythmic events and

serious non-arrhythmic complications [11]. Notably, 82.3% of our hospitalized patients who experienced SCOs presented with abnormal ECGs, reinforcing the significance of ECG abnormalities as a predictor of adverse outcomes.

These results align with the European Society of Cardiology (ESC) 2018 syncope guidelines, which recommend hospitalization for patients with syncope of unclear etiology due to the associated high risk of SCOs. An additional aspect explored in our study was the SCO rate among patients discharged with recommendations for outpatient follow-up within 24 hours. The absence of a significant increase in SCOs in this group suggests effective patient selection for discharge, highlighting the feasibility of outpatient management for those at lower risk of SCOs.

Mortality rates significantly increase in elderly patients presenting with syncope, primarily due to the multifaceted nature of potential causes and a higher prevalence of underlying cardiac conditions [12]. This correlation is supported by the research of Grossman et al., who monitored the 30-day outcomes of 293 syncope patients. Their findings revealed a mean age of 57.8 ± 24.2 years across the cohort, with patients experiencing SCOs having a mean age of 70.2 ± 21.4 years. Importantly, an age exceeding 75 years was significantly associated with SCOs [13]. Similarly, our study observed that advanced age correlated with an increased risk of SCOs, mirroring the mean age trend and reinforcing the critical consideration of age in syncope prognosis.

In a prospective analysis of syncope patients by Sarasin FP et al., 69% were found to have cardiac syncope, while the etiology remained undetermined in 14% despite comprehensive evaluations including computerized tomography (CT), troponin, plasma D-dimer, Doppler ultrasonography (USG), lung imaging, echocardiography (ECHO), and 24-hour Holter monitoring [14]. Similarly, in our study, despite employing a range of diagnostic tools such as CBT, high-sensitivity troponin T (Hs-TnT), D-Dimer, Doppler USG, and ECHO, the etiology of syncope remained elusive in 12.8% of patients following initial ED evaluation. The notably higher incidence of SCOs in hospitalized patients underscores the importance of hospitalization for those at risk, even when the specific syncope type remains unidentified through advanced ED diagnostics.

Reed MW's analysis on syncope management, supplemented by case studies, highlights the necessity for further arrhythmia investigations in patients presenting without a prodromal period, atypical syncope triggers, or facial injuries, even among younger populations [15]. This recommendation is based on the distinction between arrhythmic syncope—often lacking a prodrome or featuring a very brief prodrome of less than 3 seconds—and reflex syncope, which may have a prodrome lasting up to 3 minutes. Consistent with Reed MW's findings, our study observed a significantly higher SCO rate in patients who did not experience a prodromal period, suggesting a potential link between the absence of prodrome and increased risk of arrhythmic events.

Previous research has shown varying rates of ECG abnormalities in syncope patients, with one prospective study identifying abnormalities in 36% of cases [16], and another study reporting a 31% abnormality rate in the context of short-term SCOs [17].

Our findings align with these observations, as abnormal ECGs were detected in 26.5% of our study participants, correlating with an increased likelihood of SCOs. This concurrence with existing literature underscores the pivotal role of ECG evaluation in identifying patients at elevated risk of adverse outcomes following syncope episodes.

A comprehensive study involving 1,920 patients aged 65 and over reported that hypertension (HT) was present in 66% of the cohort, hyperlipidemia in 32%, and coronary artery disease (CAD) in another 32% [15]. Another investigation highlighted that among its participants, 32% had HT, 10% were diagnosed with diabetes mellitus (DM), 12% had CAD, and 3.9% suffered from congestive heart failure (CHF) [18]. In line with these findings, our study also identified HT, DM, CAD, and CHF among the syncope patients. However, unlike previous studies, we found no significant association between these comorbid conditions and the occurrence of SCOs in our patient population. Interestingly, our analysis did reveal that patients with malignancy were more likely to experience adverse clinical outcomes.

In a prospective study evaluating 84 patients discharged from the ED, 11% experienced a serious outcome within 7 days, identifying abnormal ECG, hematocrit below 30%, blood pressure (BP) under 90 mmHg, and a history of congestive heart failure (CHF) as key warning signs for adverse events [17]. Our study, with a higher SCO rate of 26%, also underscores the significance of ECG abnormalities and comorbidities in influencing SCOs. However, unlike the referenced study, our analysis did not find admission vital signs, hematocrit levels, or a history of CHF to be predictive of SCOs. Instead, ECG abnormalities were a more pronounced indicator of risk in our cohort. In another study focusing on ECG monitoring of 5,581 patients presenting with syncope to the ED, 7.5% encountered SCOs, attributed to various arrhythmias and device issues [19]. Consistent with these findings, AF was identified as the most frequent ECG abnormality leading to SCOs in our study, followed by ischemic ECG changes. Notably, one of the patients with a fatal outcome in our study had RBBB.

A significant study involving 282,311 individuals reported a 30-day readmission rate of 9.3%, with male gender and cardiovascular diseases highlighted as risk factors. Cardiac issues were the primary cause of readmission, accounting for 17.2% of cases [20]. While our study focused on SCOs including ED readmissions and syncope relapses within 30 days, specific causes of rehospitalization were not explored in detail. Nevertheless, cardiac etiologies were identified as the prevalent reason for initial hospital admissions in our cohort, aligning with the broader literature emphasizing cardiac conditions as a critical concern in syncope management.

Serum lactate is increasingly recognized for its role in distinguishing between syncope and other conditions causing transient loss of consciousness, such as epileptic seizures and psychogenic non-epileptic states. Matz O et al. underscored serum lactate as an exceptional biomarker for differentiating these events, advocating for its inclusion in standard evaluations [12]. Consistent with this perspective, our study found that lactate levels exceeding 2 mmol/L were significantly associated with SCOs in patients initially diagnosed with syncope after

excluding those with epilepsy. This highlights the diagnostic and prognostic importance of measuring serum lactate in the acute assessment of syncope.

Limitation

This study's limitations include its single-center design, which may limit the generalizability of the findings to broader populations and healthcare settings. Additionally, the observational nature of the study cannot establish causality between identified risk factors and serious clinical outcomes (SCOs). The reliance on initial ED evaluations and follow-up via phone calls may also introduce recall bias and underestimate the incidence of SCOs. Furthermore, the exclusion of certain patient groups, such as those under 18 and those unable to give consent, may skew the study population. Finally, the study did not account for all potential confounding variables, such as medication use or detailed medical history, which could influence the risk of SCOs.

Conclusion

This study highlights that hospitalization rates and SCOs are significantly higher among patients with cardiac syncope, abnormal ECG findings, advanced age, absence of prodromal symptoms, presence of malignancy, and elevated lactate levels at admission. These findings suggest a need for careful reevaluation of patients in the emergency department, particularly those displaying these risk factors, to improve patient outcomes. Identifying and addressing these key predictors of SCOs can guide clinicians in making more informed decisions regarding the need for hospitalization and further investigation, ultimately enhancing patient safety and care quality.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and Human Rights Statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

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Conflict of Interest

The authors declare that there is no conflict of interest.

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